

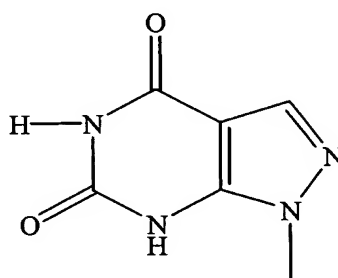
What Is Claimed Is:

1. A composition comprising a first oligomer and a second oligomer, wherein:
at least a portion of said first oligomer is capable of hybridizing with at least a portion of said second oligomer,
at least a portion of said first oligomer is complementary to and capable of hybridizing to a selected target nucleic acid, and
at least one of said first or said second oligomers includes at least one C and U or T modified binding base.
2. The composition of claim 1 wherein said first and said second oligomers are a complementary pair of siRNA oligomers.
3. The composition of claim 1 wherein said first and said second oligomers are an antisense/sense pair of oligomers.
4. The composition of claim 1 wherein each of said first and second oligomers has 12 to 50 nucleotides.
5. The composition of claim 1 wherein each of said first and second oligomers has 15 to 30 nucleotides.
6. The composition of claim 1 wherein each of said first and second oligomers has 21 to 24 nucleotides.
7. The composition of claim 1 wherein said first oligomer is an antisense oligomer.
8. The composition of claim 7 wherein said second oligomer is a sense oligomer.
9. The composition of claim 7 wherein said second oligomer has a plurality of ribose nucleotide units.

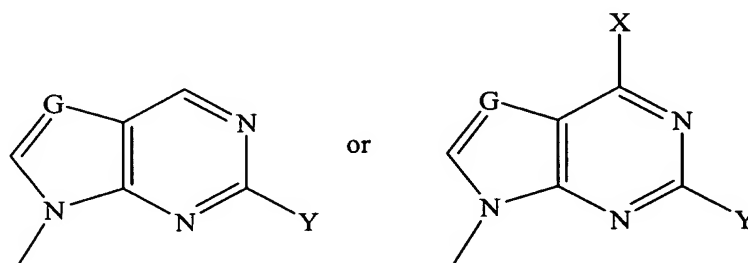
10. The composition of claim 1 wherein said first oligomer includes at least one C and U or T modified binding base.

11. The composition of claim 1 wherein said C and U or T modified binding base is a boronated C and U or T modified binding base having a boron-containing substituent selected from the group consisting of $\text{-BH}_2\text{CN}$, -BH_3 , and $\text{-BH}_2\text{COOR}$, wherein R is C1 to C18 alkyl.

12. The composition of claim 1 wherein said C and U or T modified binding base is a 1H-pyrazolo[3,4-d]pyrimidin-4(5H)-6(7H)-dione base of the following structure:



13. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein

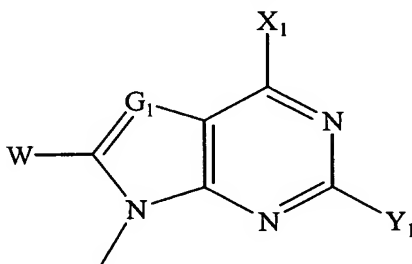
G is C or N;

X is NH_2 or OH;

Y is R_1Q or NHR_1Q , wherein R_1 is a hydrocarbonyl group having from 2 to about 20 carbon atoms and Q is H, NH_2 , a polyalkylamine, a hydrazine, a hydroxylamine, a semicarbazide, a

thiosemicarbazide, a hydrazone, a hydrazide, an imidazole, an imidazole amide, an alkyl imidazole, an alkylimidazole, a tetrazole, a triazole, a pyrrolidine, a piperidine, a piperazine, a morpholine, a thiol, an aldehyde, a ketone, an alcohol, an alkoxy group, or a halogen.

14. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

G_1 is CR_2 or N;

R_2 is H or a hydrocarbyl group having from 1 to 6 carbon atoms;

X_1 is halogen, NH_2 , OH, NHR_3Q_1 , or OR_3Q_1 ;

R_3 is H or a hydrocarbyl group having from 2 to about 20 carbon atoms;

Q_1 , Q_2 , and Q_3 are, independently, H, NH_2 , a polyalkylamine, a hydrazine, a hydroxylamine, a semicarbazide, a thiosemicarbazide, a hydrazone, a hydrazide, an imidazole, an imidazole amide, an alkyl imidazole, an alkylimidazole, a tetrazole, a triazole, a pyrrolidine, a piperidine, a piperazine, a morpholine, a thiol, an aldehyde, a ketone, an alcohol, an alkoxy group, or a halogen;

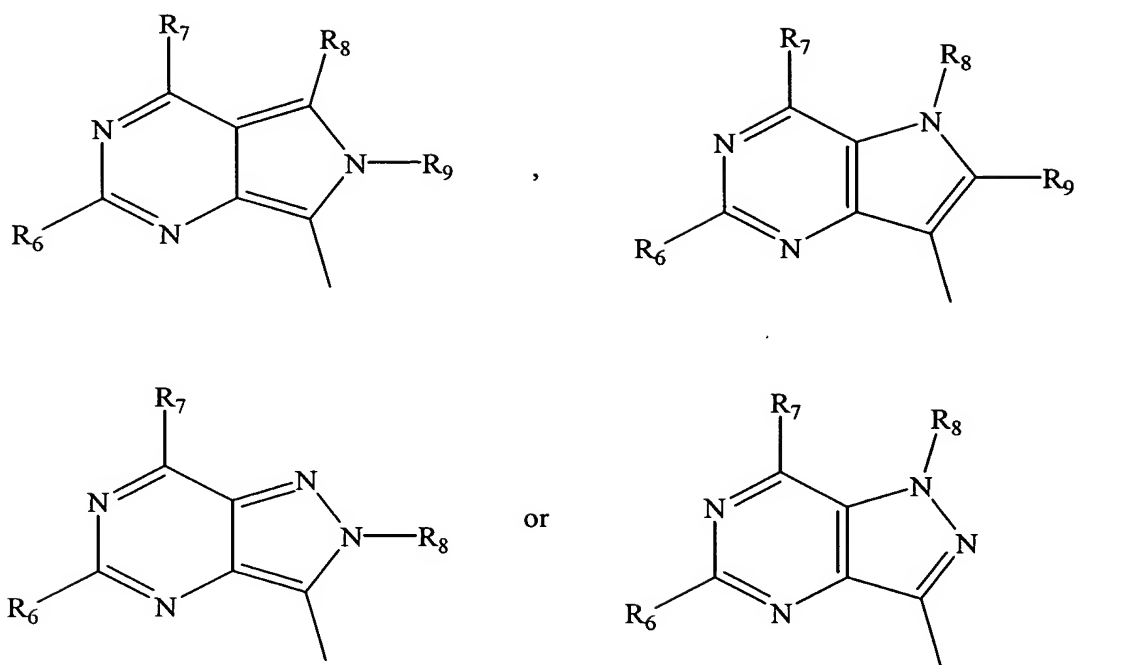
Y_1 is halogen, NH_2 , H, R_4Q_2 , or NHR_4Q_2 , wherein said R_4 is H or a hydrocarbyl group having from 2 to about 20 carbon atoms;

W is H, R_5Q_3 , or NH_4Q_3 ;

R_5 is H or a hydrocarbyl group having from 2 to about 20 carbon atoms; and

when X_1 is NH_2 and Y_1 is H or when X_1 is OH and Y_1 is NH_2 , W is other than H or G is other than N.

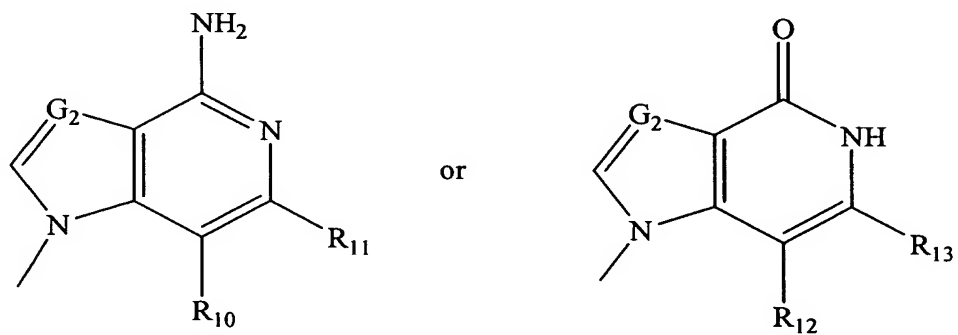
15. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein

R_6 , R_7 , R_8 , and R_9 can be the same or different and are hydrogen, halogen, hydroxy, thio or substituted thio, amino or substituted amino, carboxy, lower alkyl, lower alkenyl, lower alkynyl, aryl, lower alkyloxy, aryloxy, aralkyl, aralkyloxy or a reporter group.

16. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein

G₂ is C or N;

R₁₀ is NH₂, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino;

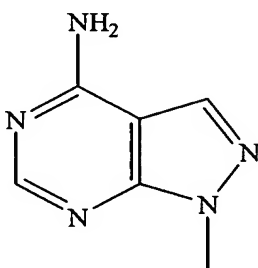
R₁₁ is alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino;

R₁₂ is H, NH₂, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino;

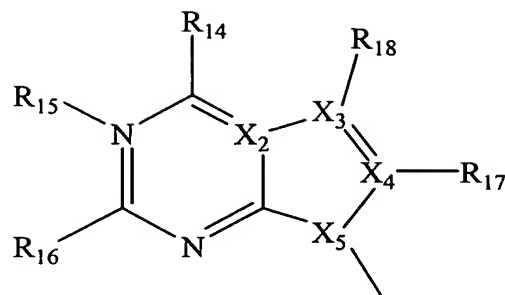
R₁₃ is NH₂, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino; and

when R₁₂ is H, R₁₃ is not NH₂.

17. The composition of claim 1 wherein said C and U or T modified binding base is a 4-amino-1H-pyrazolo[3,4-d]pyrimidine base of the following structure:



18. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

X_2 , X_3 , X_4 , and X_5 are N, O, C, S, or Si and at least one of X_2 , X_3 , X_4 , and X_5 is N;

R_{14} is a reactive group derivatizable with a detectable label wherein said reactive group is selected from the group consisting of NH_2 , SH , $=O$, a linking moiety selected from the group consisting of an amide, a thioether, a disulfide, a combination of an amide a thioether or a disulfide, $R_{19}-(CH_2)_n-R_{20}$ and $R_{19}-R_{20}-(CH_2)_n-R_{21}$ wherein n is an integer from 1 to 25 inclusive, and R_{19} , R_{20} , and R_{21} are H, OH, alkyl, acyl, amide, thioether, or disulfide, and wherein said detectable label is selected from the group consisting of radioisotopes, fluorescent or chemiluminescent reporter molecules, antibodies, haptens, biotin, photobiotin, digoxigenin, fluorescent aliphatic amino groups, avidin, enzymes, and acridinium;

R_{15} is H, absent, or part of an etheno linkage with R_{14} ;

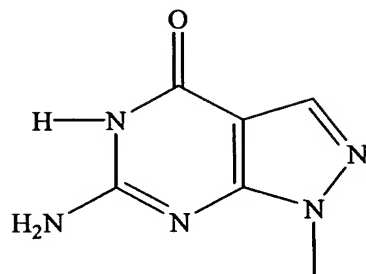
R_{16} is H, NH_2 , SH , or $=O$;

R_{17} and R_{18} are hydrogen, methyl, bromine, fluorine, iodine, alkyl or aromatic substituents, or a linking moiety selected from the group consisting of an amide, a thioether, a disulfide linkage, and a combination thereof;

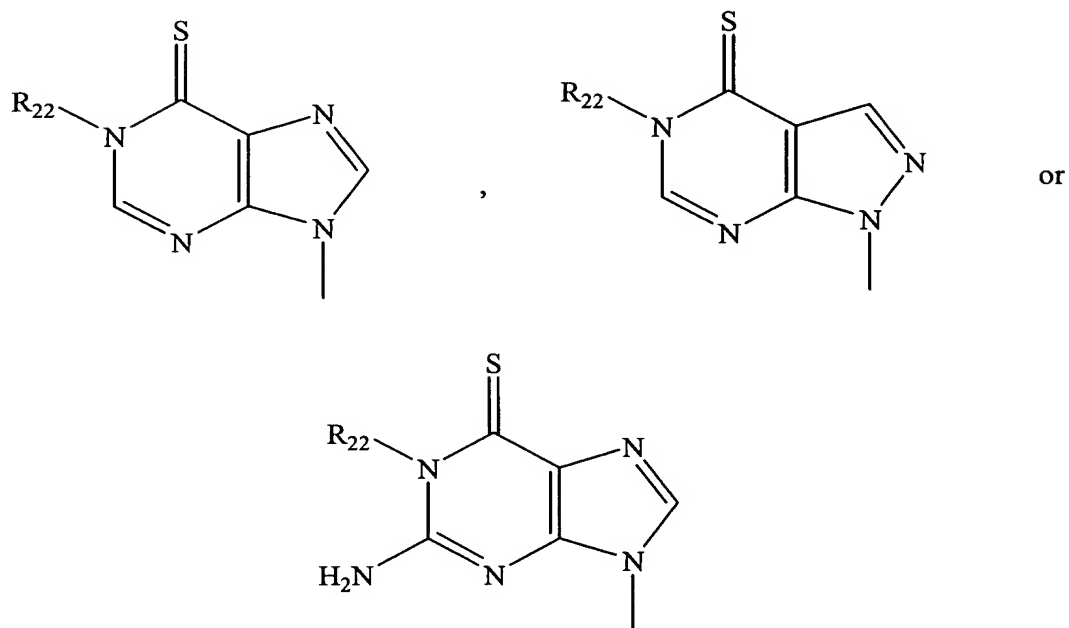
when R_{14} is NH_2 , R_{16} is H, R_{15} is absent, X_2 is C, X_3 is N, X_4 is C, X_5 is N, R_{17} is H, and R_{18} is H, then R_{17} is other than H; and

when R_{14} is $=O$, R_{16} is NH_2 , R_{15} is absent, X_2 is C, X_3 is N, X_4 is C, X_5 is N, R_{17} is H, and R_{18} is H, then R_{17} is other than H.

19. The composition of claim 1 wherein said C and U or T modified binding base is a 6-amino-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one base of the following structure:

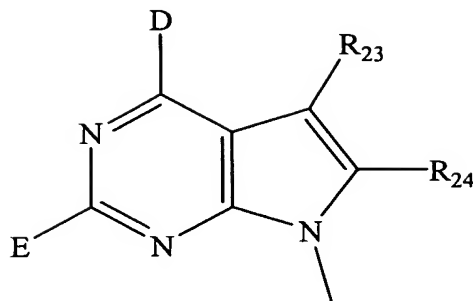


20. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein R₂₂ is C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl.

21. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

R_{23} and R_{24} are, independently of each other, 1) hydrogen; 2) halogen; 3) (C_1-C_{10}) -alkyl; 4) (C_2-C_{10}) -alkenyl; 5) (C_2-C_{10}) -alkynyl; 6) NO_2 ; 7) NH_2 ; 8) cyano; 9) $-S-(C_1-C_6)$ -alkyl; 10) $(C_1-$

$C_6)$ -alkoxy; 11) (C_6-C_{20}) -aryloxy; 12) SiH_3 ; 13) $\text{---}\overset{\overset{O}{\parallel}}{C}\text{---}R(a)$; 14) a radical as described under 3), 4) or 5) which is substituted by one or more radicals from the group SH, $S-(C_1-C_6)$ -alkyl, (C_1-C_6) -alkoxy, OH, $-NR(c)R(d)$, $-CO-R(b)$, $-NH-CO-NR(c)R(d)$, $-NR(c)R(g)$, $-NR(e)R(f)$ or $-NR(e)R(g)$, or by a polyalkyleneglycol radical of the formula $-[O-(CH_2)_r]_s-NR(c)R(d)$, where r and s are, independently of each other, an integer between 1 and 18, preferably between 1 and 6; or 15) a radical as defined under 3), 4) or 5) in which from one to all the H atoms are substituted by halogen, preferably fluorine;

$R(a)$ is OH, (C_1-C_6) -alkoxy, (C_6-C_{20}) -aryloxy, NH_2 or $NH-T$, where T is an alkylcarboxyl group or alkylamino group which is linked to one or more groups, where appropriate via a further linker, which favor intracellular uptake or serve for labeling a DNA or RNA probe or, when the oligonucleotide analog hybridizes to the target nucleic acid, attack the latter while binding, cross-linking or cleaving;

$R(b)$ is hydroxyl, (C_1-C_6) -alkoxy or $-NR(c)R(d)$;

$R(c)$ and $R(d)$ are, independently of each other, H or (C_1-C_6) -alkyl which is unsubstituted or substituted by $-NR(e)R(f)$ or $-NR(e)R(g)$;

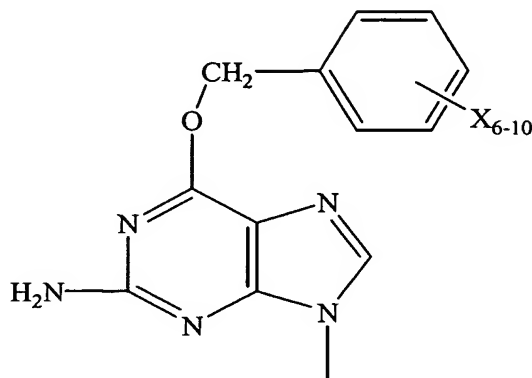
$R(e)$ and $R(f)$ are, independently of each other, H or (C_1-C_6) -alkyl;

$R(g)$ is (C_1-C_6) -alkyl-COOH;

R_{23} and R_{24} cannot each simultaneously be hydrogen, NO_2 , NH_2 , cyano or SiH_3 ; and

D and E are, independently of each other, H, OH or NH_2 .

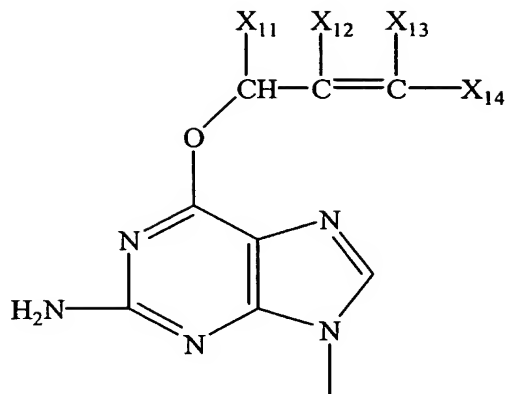
22. The composition of claim 1 wherein said C and U or T modified binding base is an O⁶-benzylguanine base of the following structure:



wherein

each of X_6 - X_{10} is selected from the group consisting of hydrogen, halogen, hydroxy, aryl, a C_1 - C_8 alkyl substituted aryl, nitro, a polycyclic aromatic alkyl containing 2-4 aromatic rings wherein the alkyl is a C_1 - C_6 , a C_3 - C_8 cycloalkyl, a C_2 - C_6 alkenyl, a C_2 - C_6 alkynyl, a C_1 - C_6 hydroxyalkyl, a C_1 - C_8 alkoxy, a C_2 - C_8 alkoxyalkyl, aryloxy, aryloxy, an acyloxyalkyl wherein the alkyl is C_1 - C_6 , amino, a monoalkylamino wherein the alkyl is C_1 - C_6 , a dialkylamino wherein the alkyl is C_1 - C_6 , acylamino, ureido, thioureido, carboxy, a carboxyalkyl wherein the alkyl is C_1 - C_6 , cyano, a cyanoalkyl wherein the alkyl is C_1 - C_6 , C-formyl, C-acyl, a dialkoxymethyl wherein the alkoxy is C_1 - C_6 , an aminoalkyl wherein the alkyl is C_1 - C_6 , and SO_nR_{25} wherein $n=0, 1, 2$ or 3 , R_{25} is H, a C_1 - C_6 alkyl or aryl.

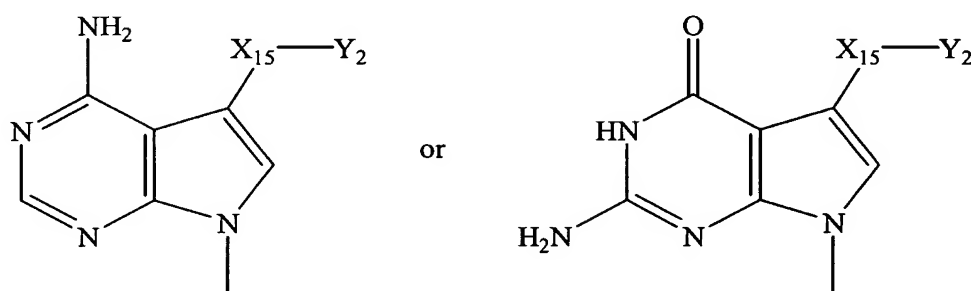
23. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

X_{11} - X_{14} are each independently selected from the group consisting of C_2 - C_8 alkoxyalkyl, aryloxy, acyloxy, acyloxyalkyl wherein the alkyl is C_1 - C_3 , hydrazino, hydroxyamino, acylamino, nitro at o, m-positions, bromine, m-methyl, C_1 - C_3 hydroxy alkyl, C_2 - C_6 alkyl, C-formyl, and aryl.

24. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



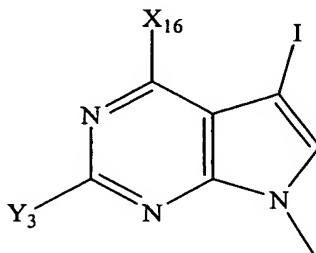
wherein

X_{15} is a linking group which is C_1 - C_{10} alkyl, C_1 - C_{10} unsaturated alkyl, dialkyl ether or dialkylthioether;

each Y_2 may be the same or different and is a cationic moiety which is $-(NH_3)^+$, $-(NH_2R_{26})^+$, $-(NHR_{26}R_{27})^+$, $-(NR_{26}R_{27}R_{28})^+$, dialkylsulfonium or trialkylphosphonium; and

R_{26} , R_{27} , and R_{28} are each independently lower alkyl having from one to ten carbon atoms.

25. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

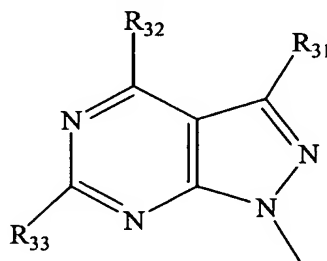
X_{16} is Cl, OH, SH, SR_{30} , OR_{29} , CN or $N(H)J$;

Y_3 is OH, SH, SR_{30} , OR_{30} , CN or $N(H)J$;

each J is, independently, hydrogen or an amino protecting group; and

each R_{29} and R_{30} is, independently, C_1 - C_{10} alkyl.

26. The composition of claim 1 wherein said C and U or T modified binding base is a pyrazolo[3,4-d]pyrimidine derivative of the following structure:



wherein

R_{31} is hydrogen or the group $-W_1-(X_{17})_{n2}-A$;

each of W_1 and X_{17} is independently a chemical linker arm;

A is an intercalator, a metal ion chelator, an electrophilic crosslinker, a photoactivatable crosslinker, or a reporter group;

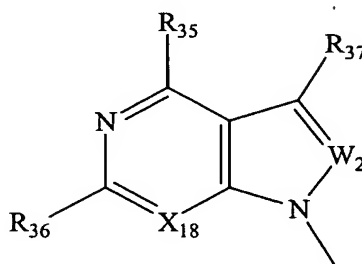
each of R_{32} and R_{33} is independently H, OR_{34} , SR_{34} , $NHOR_{34}$, NH_2 , or $NH(CH_2)_tNH_2$;

R_{34} is H or C_{1-6} alkyl;

n₂ is zero or one; and

t is zero to twelve.

27. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



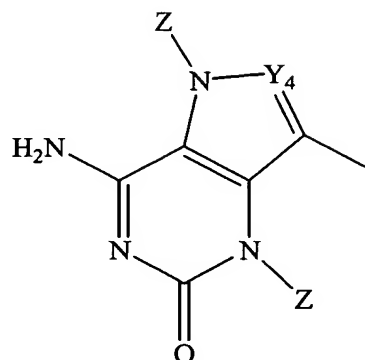
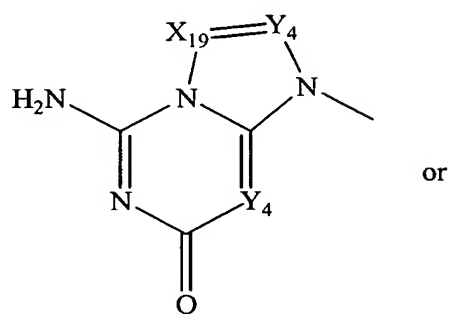
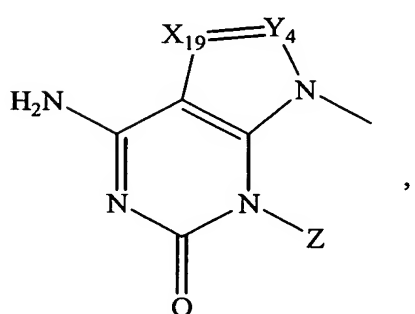
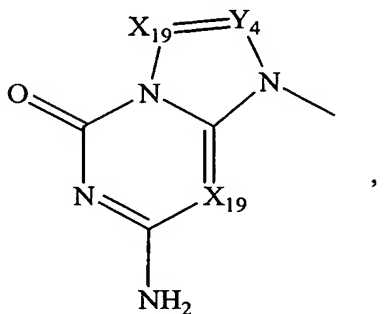
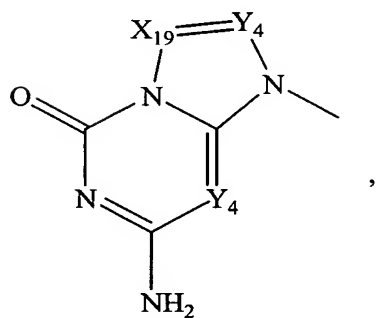
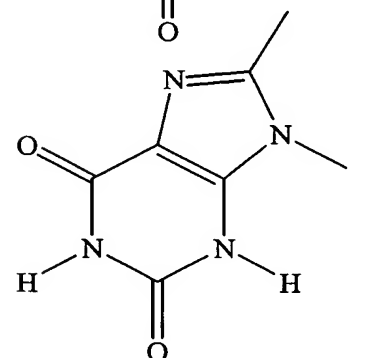
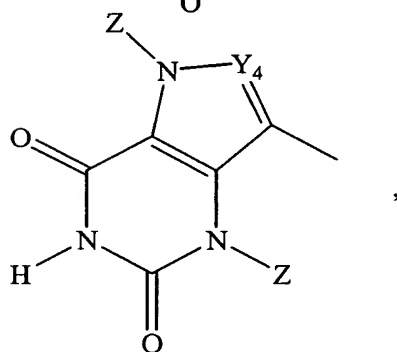
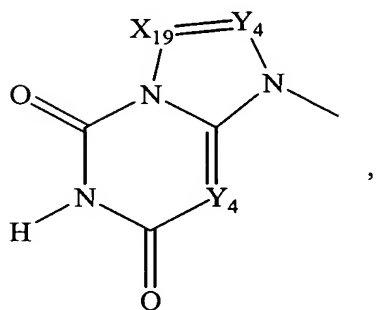
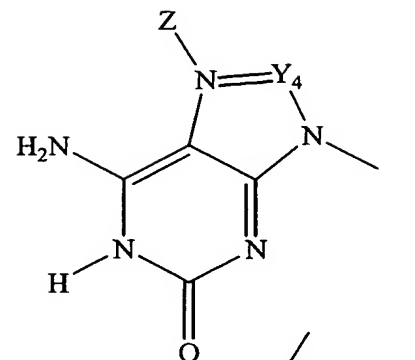
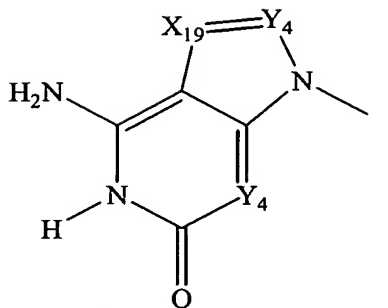
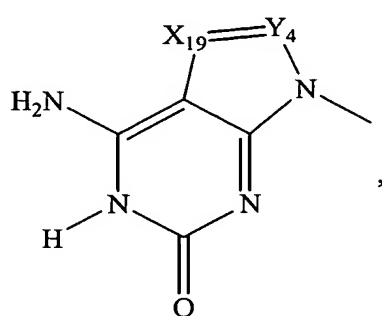
wherein

X₁₈ is a nitrogen atom or a methine radical;

W₂ is a nitrogen atom or a C-R₃₈ radical; and

R₃₅, R₃₆, R₃₇ and R₃₈, which can be the same or different, are hydrogen or halogen atoms, hydroxyl or mercapto groups, lower alkyl, lower alkylthio, lower alkoxy, aralkyl, aralkoxy or aryloxy radicals or amino groups optionally substituted once or twice.

28. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

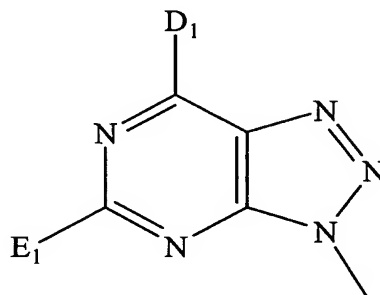
X₁₉ is selected from the group consisting of a nitrogen atom and a carbon atom bearing a substituent Z;

Z is selected from the group consisting of hydrogen and -CH₃;

Y₄ is selected from the group consisting of N and CH; and

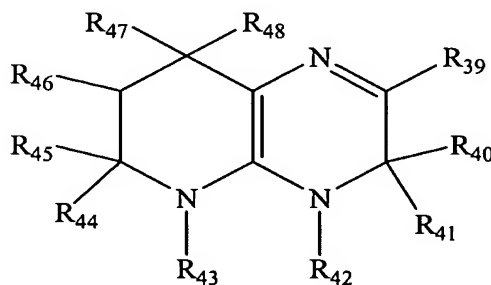
the ring structure of the purine analog comprises no more than three nitrogen atoms consecutively bonded.

29. The composition of claim 1 wherein said C and U or T modified binding base is an 8-azapurine base of the following structure:



wherein D₁ and E₁ are, independently, H, OH, or NH₂.

30. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

R₄₇ is combined with R₄₈ to form a single oxo oxygen joined by a double bond to ring vertex 4, or with R₄₆ to form a double bond between ring vertices 3 and 4;

R₄₈, when not combined with R₄₇, is either NH₂ or NH₂ either mono- or disubstituted with a protecting group;

R₄₆ when not combined with R₄₇ is a lower alkyl or H;

R₃₉ is either H, lower alkyl or phenyl;

R₄₄ is combined with R₄₅ to form a single oxo oxygen joined by a double bond to ring vertex 2, or with R₄₃ to form a double bond between ring vertices 1 and 2, such that ring vertices 2 and 4 collectively bear at most one oxo oxygen;

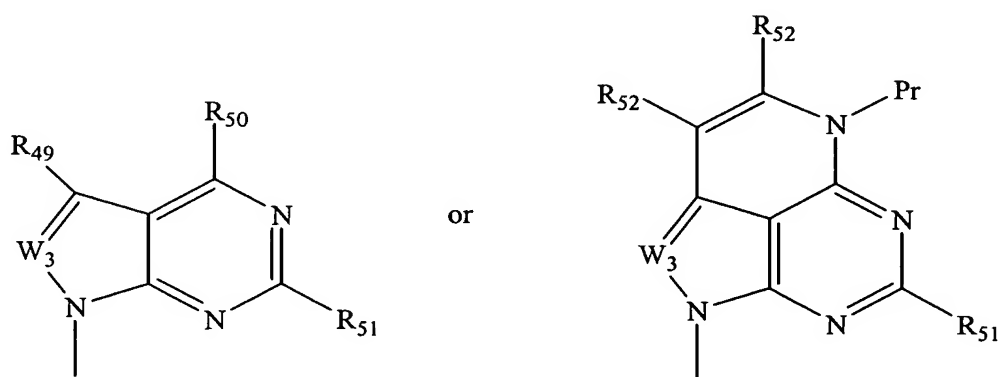
R₄₅ when not combined with R₄₄ is a member selected from the group consisting of H, phenyl, NH₂, and NH₂ mono- or disubstituted with a protecting group;

when R₄₄ is not combined with R₄₅, R₄₁ is combined with R₄₀ to form a single oxo oxygen joined by a double bond to ring vertex 7;

when R₄₄ is combined with R₄₅, R₄₁ is combined with R₄₂ to form a double bond between ring vertices 7 and 8, and R₁₉ is either H or a lower alkyl; and

R₄₃ when not combined with R₄₄, and R₄₂ when not combined with R₄₁, are a bond.

31. The composition of claim 1 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein

Pr is H (hydrogen) or a protecting group;

W₃ is CH or N;

R₄₉ is H, methyl, or a group containing a C atom connected to the 7-position of the base, wherein the C atom is bonded directly to another atom via a pi bond;

R₅₀ is OH, SH or NH₂;

R₅₁ is H, OH, SH or NH₂;

each R₅₂ is independently H, OH, CN, halogen (F, Cl, Br, I), alkyl (C1-12), alkenyl (C2-12), alkynyl (C2-12), aryl (C6-9), heteroaryl (C4-9), or both R₅₂, taken together with the carbon atoms to which they are linked at positions 11 and 12, form (a) a 5 or 6 membered carbocyclic ring or, (b) a 5 or 6 membered heterocyclic ring comprising 1-3 N, O or S ring atoms, wherein no 2 adjacent ring atoms are O-O, S-S, O-S or S-O, and wherein any unsaturated C atom of the carbocyclic or heterocyclic ring is substituted by R₅₃ and any saturated carbons contain 2 R₅₃ substituents, wherein R₅₃ is H, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), OR₅₄, SR₅₄, or N(R₅₄)₂ or halogen, and there are no more than four halogens per 5 or 6 member ring; and

R₅₄ is independently H, or alkyl (C1-4).

32. A pharmaceutical composition comprising the composition of claim 1 and a pharmaceutically acceptable carrier.

33. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with a composition of claim 1.

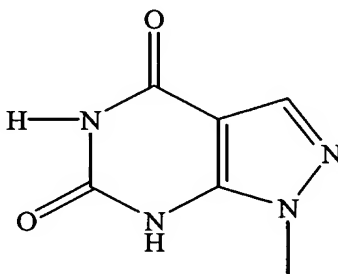
34. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of a composition of claim 1.

35. A composition comprising an oligomer complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein, said protein comprising at least a portion of a RNA-induced silencing complex (RISC), wherein:

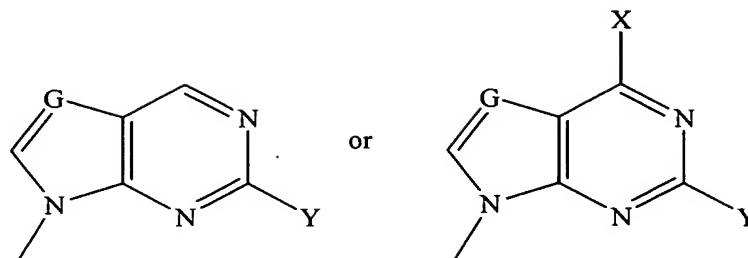
said oligomer includes at least one C and U or T modified binding base.

36. The composition of claim 35 wherein said oligomer is an antisense oligomer.

37. The composition of claim 35 wherein said oligomer has 12 to 50 nucleotides.
38. The composition of claim 35 wherein said oligomer has 15 to 30 nucleotides.
39. The composition of claim 35 wherein said oligomer has 21 to 24 nucleotides.
40. The composition of claim 35 including a further oligomer, wherein said further oligomer is complementary to and hybridizable to said oligomer.
41. The composition of claim 40 wherein said further oligomer is a sense oligomer.
42. The composition of claim 40 wherein said further oligomer is an oligomer having a plurality of ribose nucleotide units.
43. The composition of claim 35 wherein said C and U or T modified binding base is a boronated C and U or T modified binding base having a boron-containing substituent selected from the group consisting of $-\text{BH}_2\text{CN}$, $-\text{BH}_3$, and $-\text{BH}_2\text{COOR}$, wherein R is C1 to C18 alkyl.
44. The composition of claim 35 wherein said C and U or T modified binding base is a 1H-pyrazolo[3,4-d]pyrimidin-4(5H)-6(7H)-dione base of the following structure:



45. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



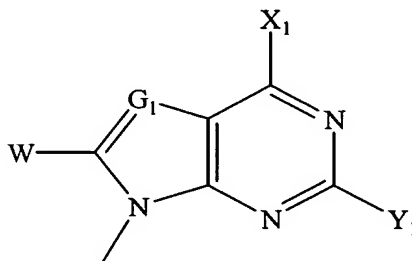
wherein

G is C or N;

X is NH₂ or OH;

Y is R₁Q or NHR₁Q, wherein R₁ is a hydrocarbyl group having from 2 to about 20 carbon atoms and Q is H, NH₂, a polyalkylamine, a hydrazine, a hydroxylamine, a semicarbazide, a thiosemicarbazide, a hydrazone, a hydrazide, an imidazole, an imidazole amide, an alkyl imidazole, an alkylimidazole, a tetrazole, a triazole, a pyrrolidine, a piperidine, a piperazine, a morpholine, a thiol, an aldehyde, a ketone, an alcohol, an alkoxy group, or a halogen.

46. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

G₁ is CR₂ or N;

R₂ is H or a hydrocarbyl group having from 1 to 6 carbon atoms;

X₁ is halogen, NH₂, OH, NHR₃Q₁, or OR₃Q₁;

R₃ is H or a hydrocarbyl group having from 2 to about 20 carbon atoms;

Q₁, Q₂, and Q₃ are, independently, H, NH₂, a polyalkylamine, a hydrazine, a hydroxylamine, a semicarbazide, a thiosemicarbazide, a hydrazone, a hydrazide, an imidazole, an imidazole amide, an alkyl imidazole, an alkylimidazole, a tetrazole, a triazole, a pyrrolidine, a

piperidine, a piperazine, a morpholine, a thiol, an aldehyde, a ketone, an alcohol, an alkoxy group, or a halogen;

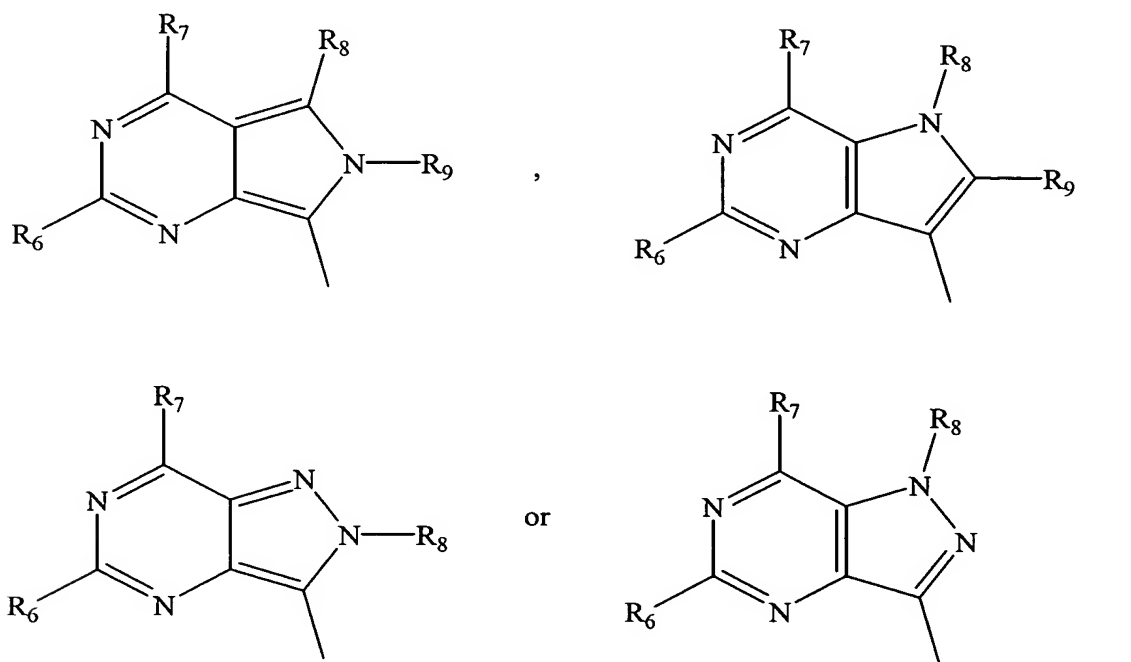
Y_1 is halogen, NH_2 , H, R_4Q_2 , or NHR_4Q_2 , wherein said R_4 is H or a hydrocarbyl group having from 2 to about 20 carbon atoms;

W is H, R_5Q_3 , or NH_4Q_3 ;

R_5 is H or a hydrocarbyl group having from 2 to about 20 carbon atoms; and

when X_1 is NH_2 and Y_1 is H or when X_1 is OH and Y_1 is NH_2 , W is other than H or G is other than N.

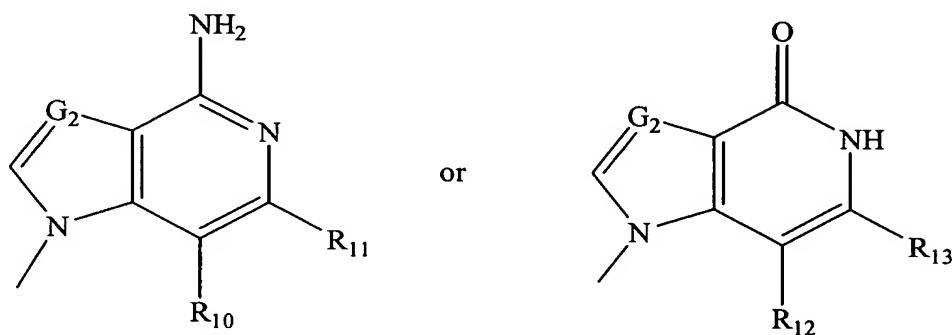
47. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein

R_6 , R_7 , R_8 , and R_9 can be the same or different and are hydrogen, halogen, hydroxy, thio or substituted thio, amino or substituted amino, carboxy, lower alkyl, lower alkenyl, lower alkynyl, aryl, lower alkyloxy, aryloxy, aralkyl, aralkyloxy or a reporter group.

48. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein

G_2 is C or N;

R_{10} is NH_2 , alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino;

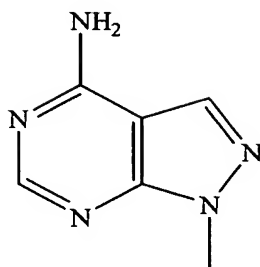
R_{11} is alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino;

R_{12} is H, NH_2 , alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino;

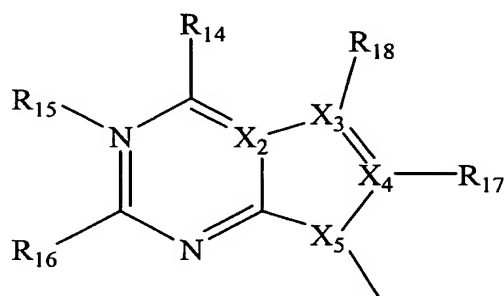
R_{13} is NH_2 , alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, amino, alkylamino, aralkylamino, substituted alkylamino, heterocycloalkyl, heterocycloalkylamino, aminoalkylamino, heterocycloalkylamino, or polyalkylamino; and

when R_{12} is H, R_{13} is not NH_2 .

49. The composition of claim 35 wherein said C and U or T modified binding base is a 4-amino-1H-pyrazolo[3,4-d]pyrimidine base of the following structure:



50. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

X_2 , X_3 , X_4 , and X_5 are N, O, C, S, or Si and at least one of X_2 , X_3 , X_4 , and X_5 is N;

R_{14} is a reactive group derivatizable with a detectable label wherein said reactive group is selected from the group consisting of NH_2 , SH , $=O$, a linking moiety selected from the group consisting of an amide, a thioether, a disulfide, a combination of an amide a thioether or a disulfide, $R_{19}-(CH_2)_n-R_{20}$ and $R_{19}-R_{20}-(CH_2)_n-R_{21}$ wherein n is an integer from 1 to 25 inclusive, and R_{19} , R_{20} , and R_{21} are H, OH, alkyl, acyl, amide, thioether, or disulfide, and wherein said detectable label is selected from the group consisting of radioisotopes, fluorescent or chemiluminescent reporter molecules, antibodies, haptens, biotin, photobiotin, digoxigenin, fluorescent aliphatic amino groups, avidin, enzymes, and acridinium;

R_{15} is H, absent, or part of an etheno linkage with R_{14} ;

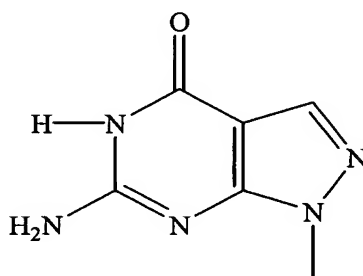
R_{16} is H, NH_2 , SH , or $=O$;

R_{17} and R_{18} are hydrogen, methyl, bromine, fluorine, iodine, alkyl or aromatic substituents, or a linking moiety selected from the group consisting of an amide, a thioether, a disulfide linkage, and a combination thereof;

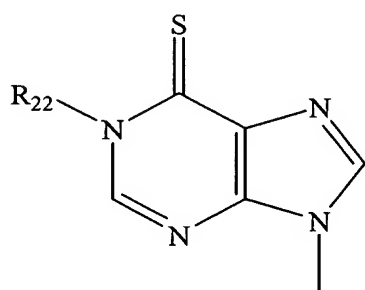
when R_{14} is NH_2 , R_{16} is H, R_{15} is absent, X_2 is C, X_3 is N, X_4 is C, X_5 is N, R_{17} is H, and R_{18} is H, then R_{17} is other than H; and

when R_{14} is $=O$, R_{16} is NH_2 , R_{15} is absent, X_2 is C, X_3 is N, X_4 is C, X_5 is N, R_{17} is H, and R_{18} is H, then R_{17} is other than H.

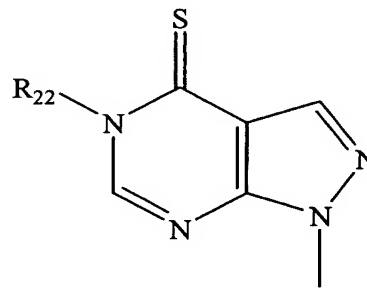
51. The composition of claim 35 wherein said C and U or T modified binding base is a 6-amino-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one base of the following structure:



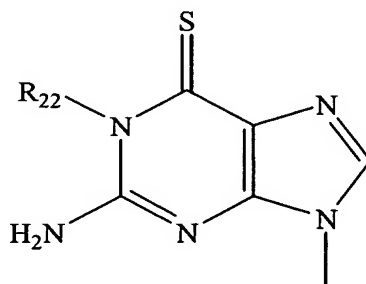
52. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



,

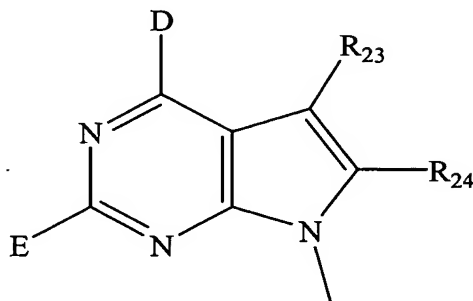


or



wherein R_{22} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl or C_2 - C_6 alkynyl.

53. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

R_{23} and R_{24} are, independently of each other, 1) hydrogen; 2) halogen; 3) (C_1-C_{10}) -alkyl; 4) (C_2-C_{10}) -alkenyl; 5) (C_2-C_{10}) -alkynyl; 6) NO_2 ; 7) NH_2 ; 8) cyano; 9) $-S-(C_1-C_6)$ -alkyl; 10) $(C_1-$

$C_6)$ -alkoxy; 11) (C_6-C_{20}) -aryloxy; 12) SiH_3 ; 13) $\text{---}\overset{\text{O}}{\parallel}{\text{C}}\text{---}R(a)$; 14) a radical as described under 3), 4) or 5) which is substituted by one or more radicals from the group SH, $S-(C_1-C_6)$ -alkyl, (C_1-C_6) -alkoxy, OH, $-NR(c)R(d)$, $-CO-R(b)$, $-NH-CO-NR(c)R(d)$, $-NR(c)R(g)$, $-NR(e)R(f)$ or $-NR(e)R(g)$, or by a polyalkyleneglycol radical of the formula $-[O-(CH_2)_r]_s-NR(c)R(d)$, where r and s are, independently of each other, an integer between 1 and 18, preferably between 1 and 6; or 15) a radical as defined under 3), 4) or 5) in which from one to all the H atoms are substituted by halogen, preferably fluorine;

$R(a)$ is OH, (C_1-C_6) -alkoxy, (C_6-C_{20}) -aryloxy, NH_2 or $NH-T$, where T is an alkylcarboxyl group or alkylamino group which is linked to one or more groups, where appropriate via a further linker, which favor intracellular uptake or serve for labeling a DNA or RNA probe or, when the oligonucleotide analog hybridizes to the target nucleic acid, attack the latter while binding, cross-linking or cleaving;

$R(b)$ is hydroxyl, (C_1-C_6) -alkoxy or $-NR(c)R(d)$;

$R(c)$ and $R(d)$ are, independently of each other, H or (C_1-C_6) -alkyl which is unsubstituted or substituted by $-NR(e)R(f)$ or $-NR(e)R(g)$;

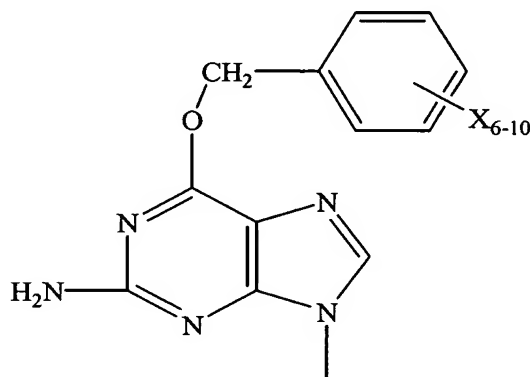
$R(e)$ and $R(f)$ are, independently of each other, H or (C_1-C_6) -alkyl;

R(g) is (C₁-C₆)-alkyl-COOH;

R₂₃ and R₂₄ cannot each simultaneously be hydrogen, NO₂, NH₂, cyano or SiH₃; and

D and E are, independently of each other, H, OH or NH₂.

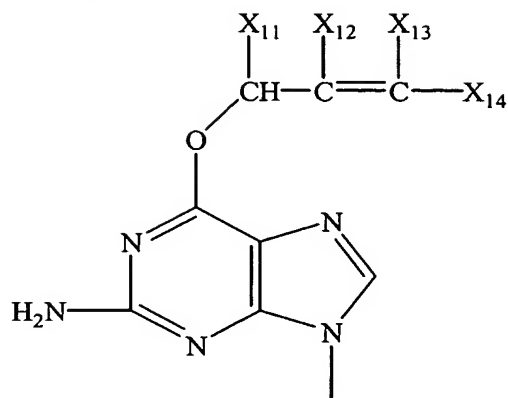
54. The composition of claim 35 wherein said C and U or T modified binding base is an O⁶ - benzylguanine base of the following structure:



wherein

each of X₆-X₁₀ is selected from the group consisting of hydrogen, halogen, hydroxy, aryl, a C₁-C₈ alkyl substituted aryl, nitro, a polycyclic aromatic alkyl containing 2-4 aromatic rings wherein the alkyl is a C₁-C₆, a C₃-C₈ cycloalkyl, a C₂-C₆ alkenyl, a C₂-C₆ alkynyl, a C₁-C₆ hydroxyalkyl, a C₁-C₈ alkoxy, a C₂-C₈ alkoxyalkyl, aryloxy, aryloxy, an acyloxyalkyl wherein the alkyl is C₁-C₆, amino, a monoalkylamino wherein the alkyl is C₁-C₆, a dialkylamino wherein the alkyl is C₁-C₆, acylamino, ureido, thioureido, carboxy, a carboxyalkyl wherein the alkyl is C₁-C₆, cyano, a cyanoalkyl wherein the alkyl is C₁-C₆, C-formyl, C-acyl, a dialkoxymethyl wherein the alkoxy is C₁-C₆, an aminoalkyl wherein the alkyl is C₁-C₆, and SO_{n1}R₂₅ wherein n1=0, 1, 2 or 3, R₂₅ is H, a C₁-C₆ alkyl or aryl.

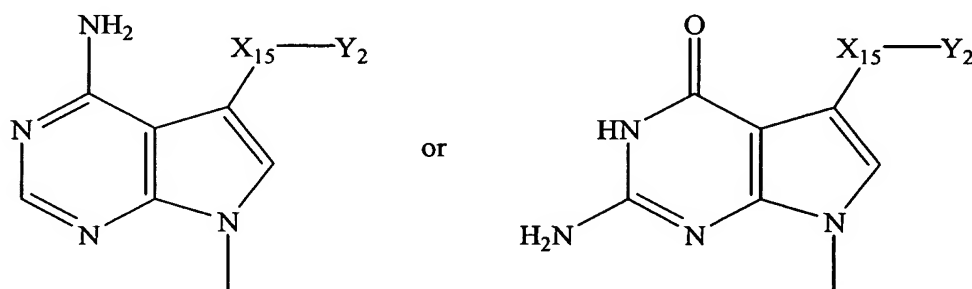
55. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

X_{11} - X_{14} are each independently selected from the group consisting of C_2 - C_8 alkoxyalkyl, aryloxy, acyloxy, acyloxyalkyl wherein the alkyl is C_1 - C_3 , hydrazino, hydroxyamino, acylamino, nitro at o, m-positions, bromine, m-methyl, C_1 - C_3 hydroxy alkyl, C_2 - C_6 alkyl, C-formyl, and aryl.

56. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



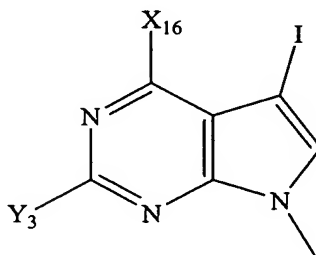
wherein

X_{15} is a linking group which is C_1 - C_{10} alkyl, C_1 - C_{10} unsaturated alkyl, dialkyl ether or dialkylthioether;

each Y_2 may be the same or different and is a cationic moiety which is $-(NH_3)^+$, $-(NH_2R_{26})^+$, $-(NHR_{26}R_{27})^+$, $-(NR_{26}R_{27}R_{28})^+$, dialkylsulfonium or trialkylphosphonium; and

R_{26} , R_{27} , and R_{28} are each independently lower alkyl having from one to ten carbon atoms.

57. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

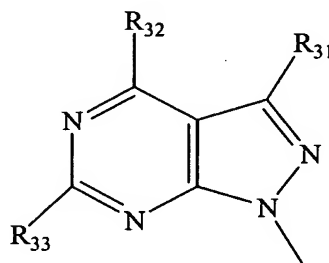
X_{16} is Cl, OH, SH, SR_{30} , OR_{29} , CN or $N(H)J$;

Y_3 is OH, SH, SR_{30} , OR_{30} , CN or $N(H)J$;

each J is, independently, hydrogen or an amino protecting group; and

each R_{29} and R_{30} is, independently, C_1 - C_{10} alkyl.

58. The composition of claim 35 wherein said C and U or T modified binding base is a pyrazolo[3,4-d]pyrimidine derivative of the following structure:



wherein

R_{31} is hydrogen or the group $-W_1-(X_{17})_{n2}-A$;

each of W_1 and X_{17} is independently a chemical linker arm;

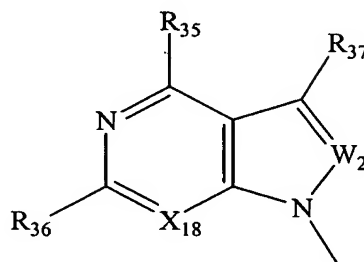
A is an intercalator, a metal ion chelator, an electrophilic crosslinker, a photoactivatable crosslinker, or a reporter group;

each of R_{32} and R_{33} is independently H, OR_{34} , SR_{34} , $NHOR_{34}$, NH_2 , or $NH(CH_2)_tNH_2$;

R_{34} is H or C_{1-6} alkyl;

n₂ is zero or one; and
t is zero to twelve.

59. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



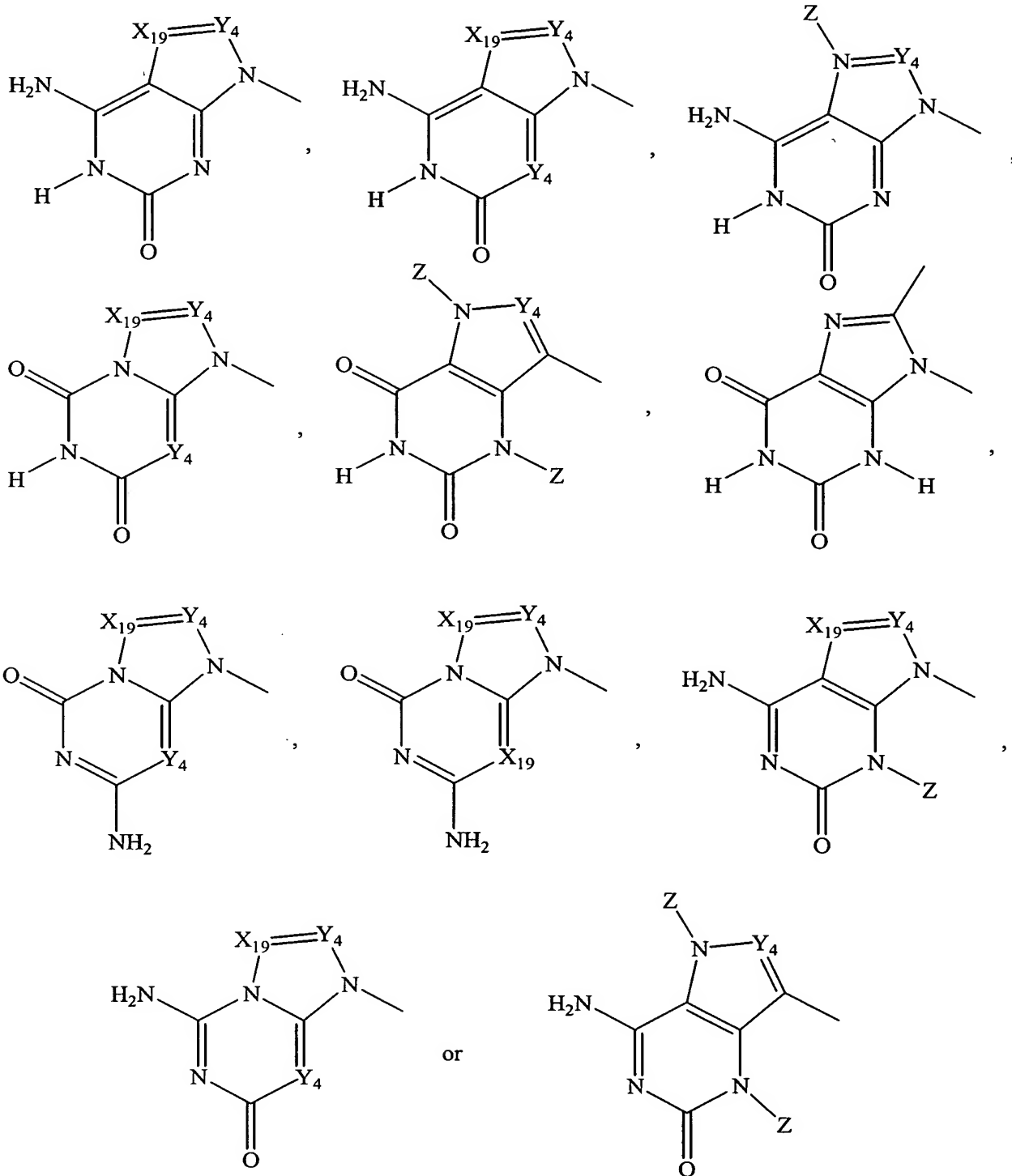
wherein

X₁₈ is a nitrogen atom or a methine radical;

W₂ is a nitrogen atom or a C-R₃₈ radical; and

R₃₅, R₃₆, R₃₇ and R₃₈, which can be the same or different, are hydrogen or halogen atoms, hydroxyl or mercapto groups, lower alkyl, lower alkylthio, lower alkoxy, aralkyl, aralkoxy or aryloxy radicals or amino groups optionally substituted once or twice.

60. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

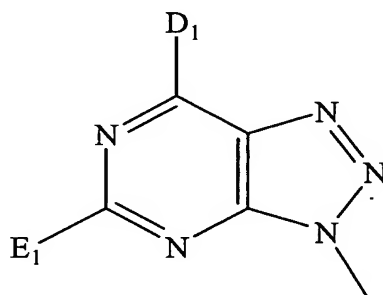
X₁₉ is selected from the group consisting of a nitrogen atom and a carbon atom bearing a substituent Z;

Z is selected from the group consisting of hydrogen and -CH₃;

Y₄ is selected from the group consisting of N and CH; and

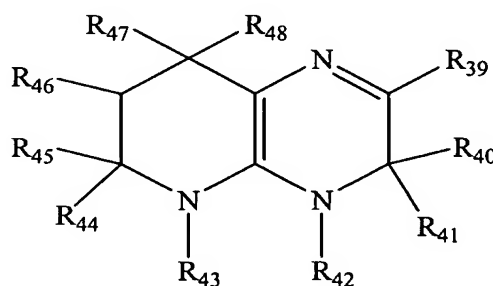
the ring structure of the purine analog comprises no more than three nitrogen atoms consecutively bonded.

61. The composition of claim 35 wherein said C and U or T modified binding base is an 8-azapurine base of the following structure:



wherein D₁ and E₁ are, independently, H, OH, or NH₂.

62. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of the following structure:



wherein

R₄₇ is combined with R₄₈ to form a single oxo oxygen joined by a double bond to ring vertex 4, or with R₄₆ to form a double bond between ring vertices 3 and 4;

R₄₈, when not combined with R₄₇, is either NH₂ or NH₂ either mono- or disubstituted with a protecting group;

R₄₆ when not combined with R₄₇ is a lower alkyl or H;

R₃₉ is either H, lower alkyl or phenyl;

R₄₄ is combined with R₄₅ to form a single oxo oxygen joined by a double bond to ring vertex 2, or with R₄₃ to form a double bond between ring vertices 1 and 2, such that ring vertices 2 and 4 collectively bear at most one oxo oxygen;

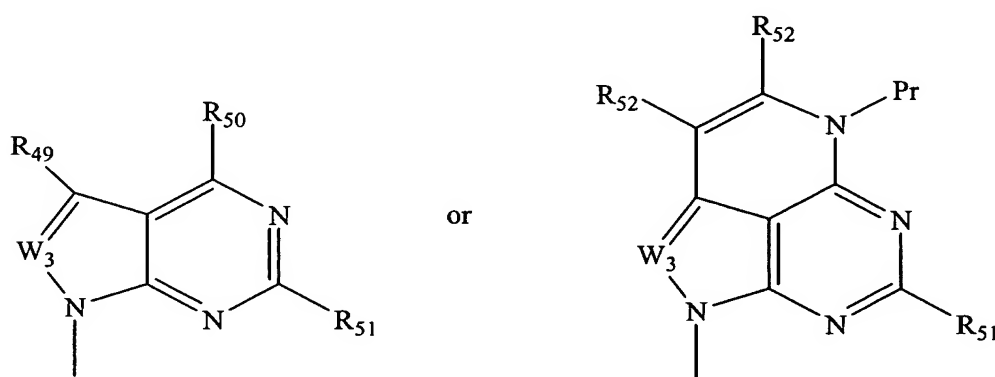
R₄₅ when not combined with R₄₄ is a member selected from the group consisting of H, phenyl, NH₂, and NH₂ mono- or disubstituted with a protecting group;

when R₄₄ is not combined with R₄₅, R₄₁ is combined with R₄₀ to form a single oxo oxygen joined by a double bond to ring vertex 7;

when R₄₄ is combined with R₄₅, R₄₁ is combined with R₄₂ to form a double bond between ring vertices 7 and 8, and R₁₉ is either H or a lower alkyl; and

R₄₃ when not combined with R₄₄, and R₄₂ when not combined with R₄₁, are a bond.

63. The composition of claim 35 wherein said C and U or T modified binding base is a C and U or T modified binding base of one of the following structures:



wherein

Pr is H (hydrogen) or a protecting group;

W₃ is CH or N;

R₄₉ is H, methyl, or a group containing a C atom connected to the 7-position of the base, wherein the C atom is bonded directly to another atom via a pi bond;

R₅₀ is OH, SH or NH₂;

R₅₁ is H, OH, SH or NH₂;

each R₅₂ is independently H, OH, CN, halogen (F, Cl, Br, I), alkyl (C1-12), alkenyl (C2-12), alkynyl (C2-12), aryl (C6-9), heteroaryl (C4-9), or both R₅₂, taken together with the carbon atoms to which they are linked at positions 11 and 12, form (a) a 5 or 6 membered carbocyclic ring or, (b) a 5 or 6 membered heterocyclic ring comprising 1-3 N, O or S ring atoms, wherein no 2 adjacent ring atoms are O-O, S-S, O-S or S-O, and wherein any unsaturated C atom of the carbocyclic or heterocyclic ring is substituted by R₅₃ and any saturated carbons contain 2 R₅₃ substituents, wherein R₅₃ is H, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), OR₅₄, SR₅₄, or N(R₅₄)₂ or halogen, and there are no more than four halogens per 5 or 6 member ring; and

R₅₄ is independently H, or alkyl (C1-4).

64. A pharmaceutical composition comprising the composition of claim 35 and a pharmaceutically acceptable carrier.

65. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with a composition of claim 35.

66. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of a composition of claim 35.